Mediterranean Journal of Clinical Psychology

ISSN 2282-1619

MJCP

Volume 9, n 2, 2021

Clinical Psychology

Interrelations between mental health, generic and thyroid-related quality of life in patients with Hashimoto's thyroiditis receiving levothyroxine replacement

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Abstract

The assessment of health-related quality of life (QoL) in chronic conditions is considered as relevant, especially in patients with hypothyroidism where a high comorbidity with depressive and anxiety issues is reported. The present cross-sectional pilot study aims at: i) examining the correlation of thyroid-specific and generic measures of QoL in patients with Hashimoto's Thyroiditis (HT); ii) investigating the associations of generic and thyroid-specific measures of QoL with depression and anxiety in patients with HT; iii) comparing generic and thyroid-specific measures of QoL in patients with HT versus controls. Twenty-one patients with serologically and/or ultrasonographically verified HT and sixteen controls with non-toxic goiter or post-surgical hypothyroidism were recruited for this study. Generic and disease-specific QoL were assessed by Health Survey Short Form-36 (SF-36) and Thyroid Patient Reported Outcome (ThyPRO) questionnaires, respectively, whereas depression and anxiety were measured through Beck Depression Inventory-second edition (BDI-II) and Hamilton Anxiety Rating Scale (HAM-A) questionnaires, respectively.

Findings showed that ThyPRO and SF-36 scores were associated with each other only regarding the mental health domain, and that such QoL measures were consistently associated with depression levels but not with anxiety. Besides, no statistically significant difference was found between patients with HT and controls with regard to generic and thyroid-specific QoL.

The present study suggests that generic and disease-specific measures of QoL can sufficiently assess the mental functioning domain and capture depressive symptoms, but only thyroid-specific measures (such as ThyPRO) can provide an accurate examination of physical aspects of QoL and the overall disease impact in patients' lives. Besides, some methodological limitations should be taken into account in both using generic and disease-specific instruments with regard to their tendency to underestimate possible anxiety problems.

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Keywords:
Clinical psychology; Depression; Anxiety; Quality of life; Hashimoto's thyroiditis.

Received: 15 May 2021
Accepted: 21 July 2021
Published: 8 August 2021

Citation: Martino, G., Caputo, A., Vicario, C. M., Feldt-Rasmussen, U., Watt, T., Vita, R., Quattropani, M. C., Benvenga, S. (2021). Interrelations between mental health, generic and thyroid-related quality of life in patients with Hashimoto's thyroiditis receiving levothyroxine replacement. *Mediterranean journal of Clinical Psychology, 9*(3). https://doi.org/10.13129/2282-1619/mjcp-3072

1. Introduction

The impact of chronic conditions in daily life represents a crucial factor to understand how patients subjectively experience their symptoms and manage them effectively (Barchetta et al., 2021; Caputo, 2014, 2020; Catalano et al., 2017, 2018, 2019, 2020; Ciprandi et al., 2017; Conversano et al., 2020b; Di Giuseppe et al., 2018; Kelly et al., 2019; Lenzo et al., 2020; Lucifora et al., 2021; Marazziti et al., 2008; Martino et al., 2018a, 2018b, 2019c, 2019d; Merlo, 2019; Mula et al., 2008; Van Houtum et al., 2015; Vicario et al., 2020). In this regard, health-related quality of life (QoL) refers to the subjective assessment of the impact of disease across several domains of functioning (e.g., physical, psychological, social, somatic) and well-being (Barofsky, 2012). The evaluation of patients' QoL is considered an integral part of clinical care to optimize their health in terms of required lifestyle changes and adjustment to disease, as well as to promote their empowerment, self-care, compliance and adherence to treatment (Aimé et al., 2020; Castelnuovo et al., 2015; Gugliandolo et al., 2020; Rosa et al., 2019; Settineri et al., 2019; Tomai et al., 2018; Watt et al., 2014). The relevance of such a construct is advocated also in the light of depression and anxiety issues, which often accompany the perceived progression of chronic conditions and the lifetime management of their related challenges (Carr-Hill, 1992; Conversano et al., 2020a; Martino et al., 2019b, 2020d; Patron et al., 2017; Quattropani et al., 2019; Randazzo et al., 2015; Vita et al., 2020).

Among the most common chronic conditions, hypothyroidism – involving the failure of the thyroid gland to produce adequate amounts of thyroid hormones – is known to affect about 5% of the adult population (Cooper & Biondi, 2012). This condition is often associated with psychopathological symptoms, such as depression (e.g., tearfulness, poor sleep, fatigue, loss of appetite) and anxiety (e.g., mental alertness, irritability, concentration problems) as residual complaints worsening health-related QoL, which patients often report after replacement treatment with levothyroxine and restoration of euthyroidism (Bianchi et al., 2004; Boesen et al., 2018a, 2018b; Cooper & Biondi, 2012; Crisanti et al., 2001; Vita et al., 2013; Winther et al., 2016).

Hashimoto's thyroiditis (HT) represents the most common type of autoimmune thyroiditis (Moncayo & Moncayo, 2014; Montagna et al., 2016; Watt et al., 2012) and the main cause of thyroid failure, characterized by symptoms of hypothyroidism (e.g., chronic fatigue, irritability, memory and cognitive problems) in about half of patients (Benvenga & Trimarchi, 2008). The high prevalence of psychopathological comorbidities (including depression and anxiety) as well as issues of distress and poor mental health of patients with HT (Broniarczyk-Czarniak, 2017; Carta et al., 2004; Markomanolaki et al., 2019; Martino et al., 2021) have raised the need to assess their QoL and deliver consistent psychological interventions (Yıldız et al., 2017).

Health-related QoL is generally assessed by generic or disease-specific standardized instruments via patient-reported outcome (PRO) measures (Patrick & Deyo, 1989). In this regard, disease-specific instruments are assumed to be more sensitive, precise and accurate since they are tailored to specific patient groups, as also reported in the field of thyroid diseases (Watt et al., 2012, 2014). The ability of generic and thyroid-specific measures of QoL to capture the subjective impact of disease in patients affected by HT and relate a possible comorbidity with depressive and anxiety issues have not been investigated much previously.

The issue of QoL impairment in patients with HT is also relevant in the light of the limitations of daily activities and reduced working capacity, since hypothyroidism represents a predictor of long-term sickness absence, disability pension and loss of labor market income (Nexo et al., 2014; Thvilum et al., 2014). As well, such patients are subject to great stress and the perception of low QoL can negatively affect disease-management, diet and lifestyle, in turn resulting in many perturbations of the immune system and clinical relapse (Markomanolaki et al., 2019).

The present cross-sectional pilot study thus aimed at: i) examining the correlation of thyroid-specific and generic measures of QoL in patients with HT; ii) investigating the associations of generic and thyroid-specific measures of QoL with depression and anxiety in patients with HT; iii) comparing generic and thyroid-specific measures of QoL in patients with HT *versus* healthy controls.

2. Materials and Methods

2.1 Participants

Patients with HT and controls were consecutively enrolled from December 2019 through March 2020 at the Department of Clinical and Experimental Medicine of the University Hospital "G. Martino" of Messina, Italy. The diagnosis of HT was based on serological and/or ultrasonographic evidence of autoimmune thyroiditis. Serological evidence was obtained through positivity for thyroglobulin antibodies (TgAb) and/or thyroid peroxidase antibodies (TPOAb), whereas ultrasonographic evidence was based on hypoechoic and/or

inhomogeneous echotexture of the thyroid. TgAb and TPOAb were measured by electroluminescence with the corresponding ECLIA kits by Roche Diagnostics (Roche Diagnostics, Switzerland), with normal values of 0–115 and 0–34 IU/mL, respectively.

All patients with HT were on replacement therapy with levothyroxine. Patients with nodular goiter or with levothyroxine-replaced post-surgical hypothyroidism were enrolled as controls. All patients with nodular goiter were euthyroid (i.e. they took neither levothyroxine nor antithyroid drugs), tested negative for both TgAb and TPOAb, and had normal thyroid echogenicity at ultrasound, while all patients who had been thyroidectomized were necessarily on levothyroxine. Patients thyroidectomized for thyroid nodules, whose serum TgAb and TPOAb were both negative prior to surgery, and whose thyroid histology demonstrated benignity of the nodule and histological absence of lymphocytic thyroidits were eligible as controls. Exclusion criteria for both HT patients and controls were: age <18 years; neuropsychiatric disturbances according to the Diagnostic and Statistical Manual of Mental Disorders diagnostic criteria (DSM-5) (American Psychiatric Association, 2013); and abnormal TSH and FT4 levels (≤0.4 or ≥4.0 mU/L, and ≤12.0 or ≥22.0 pmol/L, respectively). In this regard, controls with nodular goiter and with serum TSH between 0.4 and 1 mU/L underwent a ^{99m}Tc pertechnetate scan, were excluded if hyperfunctioning nodules were confirmed (Haugen et al., 2016). Finally, based on the mentioned exclusion criteria, only 21 patients with HT and 16 age-matched controls were eligible and entered the study.

2.2 Measures

Psychological assessment was conducted in a confidential setting by a researcher in clinical psychology, who performed a gold standard clinical psychological interview and a psychodiagnostic examination (Fava et al., 2012; Rafanelli et al., 2003).

The Italian version of the Thyroid Patient Reported Outcome (ThyPRO) questionnaire (Watt et al., 2009) was used to measure thyroid-related QoL. It comprises 84 items grouped in 13 scales and a single item measuring overall impact of thyroid disease on QoL: 4 specific symptom scales (goiter, hyperthyroid, hypothyroid, and eye symptoms), 5 non-specific scales measuring psychological states and tiredness (tiredness, cognition, anxiety, depressivity, and emotional susceptibility), and 4 thyroid disease impact scales (impaired social life, impaired daily life, impaired sex life, and cosmetic concern). Each item is scored on a five-point Likert scale from 0 (no symptoms/problems) to 4 (severe symptoms/problems). The average score of items in a scale is divided by four and multiplied by 100 to yield thirteen 0–100 scales, with higher scores indicating worse health status. In the present study, the reliability (Cronbach's α) was >.70 for all the scales.

The Italian version of the Health Survey Short Form-36 (SF-36) (Apolone & Mosconi, 1998; Ware & Sherbourne, 1992) was employed as a generic measure to assess patients' health-related QoL. It is a self-report questionnaire comprising eight domains (perceived mental health, emotional role, social functioning, vitality, general health, bodily pain, physical role, physical functioning) and with total scores ranging from 0 to 100 points, where 0 indicates maximum disability and 100 indicates no disability. SF-36 evaluates patients' health status by two synthetic indexes, the Physical Component Summary (PCS) and the Mental Component Summary (MCS), which pertain to physical and mental health, respectively. PCS and MCS values are generally expressed in t-scores with a general population mean of 50 and a standard deviation (SD) of 10, with highest values indicating better perceived health-related QoL. In the present study, the reliability (Cronbach's α) was .71 for PCS and .79 for MCS.

The Beck Depression Inventory-second edition (BDI-II) (Beck et al., 1996; Ghisi et al., 2006) was used to measure depressive symptoms. It consists of 21 items scored on a four-point Likert scale from 0 (not present) to 3 (severe), allowing the detection of both somatic-affective symptoms (e.g., agitation, loss of interest, loss of energy) and cognitive symptoms (e.g., pessimism, guilty feelings, self-dislike) of depression. Total scores of 0-13, 14-19, 20-28 and 29-63 reflect minimal, mild, moderate, and severe depression, respectively. In the present study, the reliability (Cronbach's α) was .77 for the total score, .69 for the somatic-affective component, and .70 for the cognitive component.

The Hamilton Anxiety Rating Scale (HAM-A) (Hamilton, 1959) was administered to measure anxiety symptoms. It consists of 14 items scored on a five-point Likert scale from 0 (not present) to 4 (severe) and allows the detection of psychological (e.g., anxious and depressed mood, fears, tension) and somatic symptoms (e.g., cardiovascular, respiratory or gastrointestinal symptoms). Total scores of 0-13, 14-17, 18-24, and 25-30 reflect minimal, mild, moderate, and severe anxiety, respectively. In the present study, the reliability (Cronbach's α) was .69 for the total score, .66 for the psychic component, and .61 for the somatic component.

2.3 Statistical Analysis

Statistical analysis was performed using IBM SPSS, version 25 for Windows. To address the first research aim, non-parametric correlations (Spearman's Rho) were performed to examine the associations of ThyPRO scales with both SF-36 PCS and MCS. To address the second research aim, non-parametric correlations were also employed to evaluate the associations of the thyroid-specific and generic measures of QoL with BDI-II and HAM-A scores.

Finally, non-parametric independent samples tests (Mann-Whitney's U) were conducted to compare patients with HT and controls by both ThyPRO scales and SF-36 PCS and MCS. Given the presence of multiple comparisons that could inflate type I error (false positives), we further considered the effect size (and relative confidence intervals [CI]) of the observed relationships/differences through *r* values, with cutoffs of .1, .3, and .5 indicating small, medium, and large effect sizes (Cohen, 1988).

2.4 Ethics Statement

The study was approved by the Ethical Committee of the University Hospital "G. Martino", Messina, Italy, protocol identifying number 80/19, 16/09/2019. This study complies with the 1964 Helsinki declaration and its later amendments. All participants were adequately informed about the scientific purpose of the study and gave their informed written consent. All data were analyzed anonymously.

3. Results

Overall 78.4% were women, with a mean age of 58.1 (*SD* =12.3) and had secondary or higher education level in most of cases (78.4%). No statistically significant differences were found between patients with HT and controls by gender (p = .055), age (p = .946) and education level (p = .898), nor by serum TSH (p = .700) and FT4 concentrations (p = .960). This lack of statistical difference in thyroid function tests underlies the euthyroid status of the patient group. Of the 21 patients with HT, 14 (66.7%) were positive for both antibodies (TgAb and TPOAb), 6 patients (28.6%) were negative for both TgAb and TPOAb, and one patient (4.8%) for only TgAb. All the recruited 21 patients had the typical ultrasound features of HT, namely a hypoechoic and inhomogeneous thyroid parenchyma, except for three patients, who were positive for both antibodies.

Descriptive statistics of the psychological measures for HT and control groups are shown in Table 1. On average, the worst ThyPRO scores were tiredness, anxiety, depressivity, and emotional susceptibility as scales pertaining to the mental health domain in both clinical and control group. This finding seemed confirmed also when considering health-related QoL since mean MCS scores were one standard deviation below the mean of healthy Italian controls (<40) (Apolone & Mosconi, 1998). All patients with HT and controls reported mild depression (with an overall score between 13 and 19) according to the Italian norms for the BDI-II (Ghisi et al., 2006). In contrast, anxiety levels ranged from moderate to severe because the mean HAM-A score was >17 for the HT group and >24 for controls (Table 1).

Table 1. Descriptive statistics of the study measures (N=37)

	HT group (n = 21)		Control group (n = 16)	
Measure	Mean	Std. Deviation	Mean	Std. Deviation
Goiter symptoms (ThyPRO)	17.64	20.75	22.30	23.77
Hyperthyroid symptoms (ThyPRO)	21.88	14.66	32.82	17.90
Hypothyroid symptoms (ThyPRO)	38.39	26.46	44.14	21.10
Eye symptoms (ThyPRO)	24.11	19.72	25.39	21.59
Tiredness (ThyPRO)	58.16	20.11	55.13	22.77
Cognitive Complaints (ThyPRO)	28.57	19.86	41.41	27.49
Anxiety (ThyPRO)	48.21	24.24	54.43	20.78
Depressivity (ThyPRO)	45.07	22.88	50.22	27.49
Emotional susceptibility (ThyPRO)	48.15	23.18	48.78	21.11
Impaired social life (ThyPRO)	13.39	24.71	15.63	16.46
Impaired daily life (ThyPRO)	18.85	17.81	29.43	24.32
Impaired sex life (ThyPRO)	32.14	34.81	38.28	27.94
Cosmetic concern (ThyPRO)	25.79	28.12	11.98	18.93
Overall quality of life (ThyPRO)	20.24	25.76	10.94	20.35
PCS	42.90	12.48	41.69	9.78
MCS	32.81	12.97	35.06	11.97
BDI-II (Total)	17.95	7.54	19.56	9.32
BDI-II (Somatic-Affective)	12.95	5.30	13.69	6.16
BDI-II (Cognitive)	5.00	3.70	5.87	4.33
HAM-A (Total)	23.90	7.47	25.00	6.40
HAM-A (Psychic)	12.43	4.64	13.19	4.04
HAM-A (Somatic)	11.48	4.30	11.81	3.47

Note. ThyPRO (Thyroid Patient Reported Outcome), PCS (Physical Component Summary), MCS (Mental Component Summary), BDI-II (Beck Depression Inventory II Version), HAM-A (Hamilton Anxiety Rating Scale).

Some statistically significant correlations between generic and thyroid-related measures of QoL were found in patients with HT.

Thus, PCS from SF-36 correlated with issues of emotional susceptibility (r = .56, p <.01, 95% CI [.01, .80]), whereas, MCS from SF-36 was negatively associated with: hyperthyroid symptoms (r = -.62, p <.01, 95% CI [-.83, -.26]), tiredness (r = -.49, p <.05, 95% CI [-.76, -.08]), cognitive complaints (r = -.48, p <.05, 95% CI [-.76, -.06]), anxiety (r = -.58, p <.01, 95% CI [-.81, -.20]), depressivity (r = -.77, p <.001, 95% CI [-.90, -.51]), emotional susceptibility (r = -.76, p <.001, 95% CI [-.90, -.49]), and impaired daily life (r = -.44, p <.05, 95% CI [-.73, -.01]) (see Table 2).

Table 2. Correlations between generic (SF-36) and thyroid-related (ThyPRO) measures of QoL in patients with HT (n=21)

	PCS		MCS	
	Spearman's rho	p-value	Spearman's rho	p-value
Goiter symptoms (ThyPRO)	-.26	.248	-.19	.412
Hyperthyroid symptoms (ThyPRO)	.05	.828	-.62	.003
Hypothyroid symptoms (ThyPRO)	-.08	.743	-.04	.851
Eye symptoms (ThyPRO)	-.36	.110	-.20	.375
Tiredness (ThyPRO)	-.39	.084	-.49	.024
Cognitive Complaints (ThyPRO)	.03	.880	-.48	.027
Anxiety (ThyPRO)	.40	.069	-.58	.005
Depressivity (ThyPRO)	.12	.603	-.77	< .001
Emotional susceptibility (ThyPRO)	.56	.009	-.76	< .001
Impaired social life (ThyPRO)	.33	.144	-.14	.531
Impaired daily life (ThyPRO)	-.13	.574	-.44	.045
Impaired sex life (ThyPRO)	-.08	.715	.16	.475
Cosmetic concern (ThyPRO)	.11	.642	-.25	.266
Overall quality of life (ThyPRO)	.13	.583	-.06	.788

Note. ThyPRO (Thyroid Patient Reported Outcome), PCS (Physical Component Summary), MCS (Mental Component Summary).

Overall depression was found to correlate with many scales of ThyPRO related to hyperthyroid symptoms (r = .58, p <.01, 95% CI [.19, .81]), tiredness (r = .46, p <.05, 95% CI [.03, .74]), cognitive complaints (r = .49, p <.05, 95% CI [.07, .76]), anxiety (r = .53, p <.05, 95% CI [.12, .78]), depressivity (r = .81, p <.001, 95% CI [.58, .92]), emotional susceptibility (r = .68, p <.001,

95% CI [.35, .86]), and impaired daily life (r = .44, p <.05, 95% CI [.01, .73]). Then, a further association emerged between the cognitive component of depression and cosmetic concern (r = .46, p <.05, 95% CI [.03, .74]). However, better mental health derived from generic (SF-36) health-related QoL was strongly associated with lower depression (r = -.82, p <.001, 95% CI [-.92, -.60]) (see Table 3).

Table 3. Associations between generic (SF-36) and thyroid-related (ThyPRO) measures of QoL, respectively and depression (BDI-II) in patients with HT (n=21)

	BDI-II (Total)		BDI-II (Somatic-Affective)		BDI-II (Cognitive)	
	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value
Goiter symptoms (ThyPRO)	.11	.624	.22	.344	-.00	.993
Hyperthyroid symptoms (ThyPRO)	.58	.006	.46	.036	.43	.049
Hypothyroid symptoms (ThyPRO)	-.02	.917	-.18	.428	.11	.631
Eye symptoms (ThyPRO)	.24	.291	.20	.372	.26	.258
Tiredness (ThyPRO)	.46	.038	.51	.018	.23	.308
Cognitive Complaints (ThyPRO)	.49	.025	.30	.187	.55	.009
Anxiety (ThyPRO)	.53	.014	.38	.088	.51	.019
Depressivity (ThyPRO)	.81	< .001	.73	< .001	.63	.002
Emotional susceptibility (ThyPRO)	.68	< .001	.53	.014	.64	.002
Impaired social life (ThyPRO)	.20	.372	.03	.881	.28	.215
Impaired daily life (ThyPRO)	.44	.046	.37	.098	.39	.077
Impaired sex life (ThyPRO)	-.13	.571	-.04	.850	-.10	.665
Cosmetic concern (ThyPRO)	.18	.441	-.03	.900	.46	.036
Overall quality of life (ThyPRO)	-.01	.972	-.18	.429	.28	.216
PCS	.24	.294	.05	.825	.29	.197
MCS	-.82	<.001	-.66	.001	-.72	<.001

Note. ThyPRO (Thyroid Patient Reported Outcome), PCS (Physical Component Summary), MCS (Mental Component Summary), BDI-II (Beck Depression Inventory II Version).

Positive associations were found between ThyPRO scales and anxiety in relation with hyperthyroid symptoms (r = .45, p <.05, 95% CI [.02, .74]) and tiredness (r = .45, p <.05, 95% CI [.02, .74]); whereas no association was detected regarding generic health-related QoL (see Table 4).

Table 4. Associations between generic (SF-36) and thyroid-related (ThyPRO) measures of QoL and anxiety in patients with HT (n=21)

	HAM-A (Total)		HAM-A (Psychic)		HAM-A (Somatic)	
	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value
Goiter symptoms (ThyPRO)	.18	.445	-.01	.975	.40	.076
Hyperthyroid symptoms (ThyPRO)	.45	.040	.35	.122	.33	.144
Hypothyroid symptoms (ThyPRO)	.10	.654	.09	.709	.10	.661
Eye symptoms (ThyPRO)	.18	.435	.08	.734	.31	.171
Tiredness (ThyPRO)	.45	.040	.35	.116	.32	.150
Cognitive Complaints (ThyPRO)	.39	.082	.36	.107	.26	.260
Anxiety (ThyPRO)	.13	.576	.20	.387	.02	.937
Depressivity (ThyPRO)	.16	.476	.20	.374	.05	.825
Emotional susceptibility (ThyPRO)	.20	.394	.31	.167	-.00	.991
Impaired social life (ThyPRO)	-.23	.311	-.12	.598	-.23	.312
Impaired daily life (ThyPRO)	.22	.345	.31	.173	.07	.762
Impaired sex life (ThyPRO)	-.03	.907	-.10	.658	.10	.665
Cosmetic concern (ThyPRO)	.05	.833	.10	.675	.04	.875
Overall quality of life (ThyPRO)	-.22	.326	-.12	.603	-.18	.425
PCS	-.14	.532	.06	.784	-.35	.117
MCS	-.30	.183	-.30	.180	-.11	.633

Note. ThyPRO (Thyroid Patient Reported Outcome), PCS (Physical Component Summary), MCS (Mental Component Summary), HAM-A (Hamilton Anxiety Rating Scale).

Finally, there was no significant difference in generic and thyroid-related measures of QoL between patients with HT and controls (Table 5).

Table 5. Differences between patients with HT and controls on generic (SF-36) and thyroid-related (ThyPRO) measures of QoL (n=37)

				95% CI for Rank-Biserial Correlation	
	U	p	Rank-Biserial Correlation	Lower	Upper
Goiter symptoms (ThyPRO)	191.5	.479	0.14	-0.23	0.48
Hyperthyroid symptoms (ThyPRO)	228.0	.067	0.36	-0.01	0.64
Hypothyroid symptoms (ThyPRO)	187.0	.569	0.11	-0.26	0.46
Eye symptoms (ThyPRO)	173.0	.890	0.03	-0.34	0.39
Tiredness (ThyPRO)	156.0	.724	-0.07	-0.42	0.30
Cognitive Complaints (ThyPRO)	214.0	.162	0.27	-0.01	0.58
Anxiety (ThyPRO)	192.0	.470	0.14	-0.23	0.48
Depressivity (ThyPRO)	185.5	.601	0.10	-0.27	0.45
Emotional susceptibility (ThyPRO)	173.0	.890	0.03	-0.34	0.39
Impaired social life (ThyPRO)	205.5	.222	0.22	-0.15	0.54
Impaired daily life (ThyPRO)	207.0	.234	0.23	-0.14	0.55
Impaired sex life (ThyPRO)	195.0	.408	0.16	-0.21	0.49
Cosmetic concern (ThyPRO)	124.5	.175	-0.26	-0.57	0.11
Overall quality of life (ThyPRO)	132.0	.209	-0.21	-0.54	0.16
PCS	162.00	.866	-0.04	-0.39	0.33
MCS	185.00	.612	0.10	-0.27	0.45

Note. ThyPRO (Thyroid Patient Reported Outcome), PCS (Physical Component Summary), MCS (Mental Component Summary).

4. Discussion

In this study, mean SF-36, BDI-II and HAM-A scores revealed low mental health-related QoL, mild depression, and moderate anxiety in patients with HT compared to a normal Italian population. Issues of psychological suffering were also confirmed by the ThyPRO scales measuring psychological states and tiredness, which showed worse scores. This finding is in line with previous research indicating that patients with autoimmune hypothyroidism have poor

QoL, especially in terms of psychological symptoms (Watt et al., 2012), and tend to report depression and anxiety symptoms (Bathla et al., 2016; Bauer et al., 2001; Bell et al., 2007; Grabe et al., 2005; Rieben et al., 2016; Samuels, 2008).

The lack of associations found between ThyPRO and SF-36 scores highlight that SF-36 PCS did not succeed in capturing physical symptoms and functioning, thus suggesting the reduced sensitivity and accuracy of generic measures of QoL in patients with HT. However, SF-36 MCS was associated with a higher number of ThyPRO scales dealing with the mental health domain to a moderate to high extent, despite failing to account for thyroid disease impact (except for impaired daily life), thus suggesting the methodological strengths of thyroid-related measures to provide a more exhaustive evaluation of patient QoL (Watt et al., 2012, 2014, 2015; Wong et al., 2016, 2018).

Both ThyPRO and SF-36 MCS scores were consistently related to depression levels (obtained from BDI-II) to a very high extent, in accordance with the found comorbidity with depression, especially in the presence of impaired health-related QoL (Dayan & Panicker, 2013; Djurovic et al., 2018). The possibility to focus depression issues when assessing QoL is particularly important since depression levels in patients with HT tend to predict a lower reliance on problem-focused coping style (Yıldız et al., 2017). Indeed, when failing to elaborate on disease-related depressive feelings, patients affected by chronic conditions tend to enact disengagement strategies preventing from self-care and treatment adherence (Caputo, 2013, 2019a, 2019b; Di Giuseppe et al., 2019, 2020; Marchini et al., 2018, 2020; Martino et al., 2020a).

However, no association was detected between such QoL measures and anxiety symptoms. Thus, only ThyPRO scales of hyperthyroid symptoms and tiredness correlated moderately with the HAM-A total score, probably due to some overlapping items dealing with exhaustion, tension and somatic manifestations. The reduced suitability of the used measures to grasp anxiety issues may represent one of the major limitations of QoL instruments, to be addressed in future health-related QoL research. Indeed, the improvement of patients with HT' lifestyle and health status may depend on the ability for early detection of anxiety issues and providing stress-management interventions (Markomanolaki et al., 2019; Mizokami et al., 2004).

Finally, no difference was found between patients with HT and controls in either ThyPRO or SF-36 scores, despite previous findings showing that patients with HT reported more anxiety and depression compared to euthyroid controls (Djurovic et al., 2018). However, the small sample sizes of the HT and control groups may have prevented statistically significant differences.

Overall, the present study highlights the presence of psychological issues potentially affecting QoL of patients with HT, suggesting the relevance of psychological interventions addressed to this target population. In this regard, emotion recognition is considered as a relevant factor preventing disease-related distress and improving health status in many chronic conditions (Conversano & Di Giuseppe, 2021; Di Giuseppe et al., 2014; Martino et al., 2019a, 2020b, 2020c; Craparo et al., 2016; Palagini et al., 2016; Piccinni et al., 2012; Veltri et al., 2012; Vicario, 2013; Vicario et al., 2021), as in thyroid diseases (Le Donne et al., 2012). Impaired emotional capacity has been suggested as a risk factor for HT development and a predictor of HT course (Hasegawa et al., 2019; Ivanova & Gorobets, 2011).

In drawing conclusions from this study, some limitations have to be considered such as the small sample size, the cross-sectional design, the use of self-reported measures, and the lack of subgroup analyses, which prevent generalization of the findings and establishment of causal relationships among the studied variables. This notwithstanding, the added value of this study refers to providing a novel piece of research about QoL of patients with HT, adopting generic and thyroid-related measures along with a gold standard clinical psychological interview. In terms of practical and clinical implications, an accurate and timely QoL assessment may be fruitful to identify some key factors for promoting better patient well-being and functioning in both social and work life (Nexo et al., 2014; Yalcin et al., 2017). As well, future studies could address the impact of emotional regulation in protecting patients from disease-related distress such as depression and anxiety and assess defense mechanisms potentially preventing from self-care and treatment adherence with appropriate measures.

In conclusion generic and disease-related measures of QoL can sufficiently assess the mental functioning domain and capture depressive symptoms, but only thyroid-related measures (like ThyPRO) can provide an accurate examination of physical functioning and the overall disease impact in patients' lives. Besides, some methodological limitations should be taken into account in both using generic and disease-specific instruments with regard to their tendency to underestimate possible anxiety problems.

Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any potential conflict of interest.

References

1. Aimé, A., Fuller-Tyszkiewicz, M., Dion, J., Markey, C. H., Strodl, E., McCabe, M., Mellor, D., Granero Gallegos, A., Pietrabissa, G., Alcaraz-Ibánez, M., Bégin, C., Blackburn, M., Caltabiano, M., Castelnuovo, G., Gullo, S., Hayami-Chisuwa, N., He, Q., Lo Coco, G., Manzonie, G. M., … Maïano, C. (2020). Assessing positive body image, body satisfaction, weight bias, and appearance comparison in emerging adults: A cross-validation study across eight countries. *Body Image*, *35*, 320-332. https://doi.org/10.1016/j.bodyim.2020.09.014
2. American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders (DSM-5®)*. American Psychiatric Pub.
3. Apolone, G., & Mosconi, P. (1998). The Italian SF-36 Health Survey: Translation, validation and norming. *Journal of clinical epidemiology, 51*(11), 1025-1036.
4. Barchetta, S., Martino, G., Craparo, G., Salehinejad, M. A., Nitsche, M. A., & Vicario, C. M. (2021). Alexithymia is linked with a negative bias for past and current events in healthy humans. *International Journal of Environmental Research and Public Health*, *18*(13), 6696. https://doi.org/10.3390/ijerph18136696
5. Barofsky, I. (2012). *Quality: its definition and measurement as applied to the medically ill*. Springer.
6. Bathla, M., Singh, M., & Relan, P. (2016). Prevalence of anxiety and depressive symptoms among patients with hypothyroidism. *Indian Journal of Endocrinology and Metabolism*, *20*(4), 468-474.
7. Bauer, M., Priebe, S., Berghöfer, A., Bschor, T., Kiesslinger, U., & Whybrow, P. C. (2001). Subjective response to and tolerability of long-term supraphysiological doses of levothyroxine in refractory mood disorders. *Journal of affective disorders*, *64*(1), 35-42. https://doi.org/10.1016/S0165-0327(00)00215-9
8. Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for the Beck depression inventory-II*. Psychological Corporation.
9. Bell, R. J., Rivera-Woll, L., Davison, S. L., Topliss, D. J., Donath, S., & Davis, S. R. (2007). Well-being, health-related quality of life and cardiovascular disease risk profile in women with subclinical thyroid disease - a community-based study. *Clinical Endocrinology*, 66(4), 548–556. https://doi.org/10.1111/j.1365-2265.2007.02771.x
10. Benvenga, S., & Trimarchi, F. (2008). Changed presentation of Hashimoto's thyroiditis in North-Eastern Sicily and Calabria (Southern Italy) based on a 31-year experience. *Thyroid*, *18*(4), 429-441. https://doi.org/10.1089/thy.2007.0234
11. Bianchi, G. P., Zaccheroni, V., Solaroli, E., Vescini, F., Cerutti, R., Zoli, M., & Marchesini, G. (2004). Health-related quality of life in patients with thyroid disorders. *Quality of Life Research*, *13*(1), 45-54. https://doi.org/10.1023/B:QURE.0000015315.35184.66
12. Boesen, V. B., Feldt-Rasmussen, U., Bjorner, J. B., Cramon, P., Groenvold, M., Nygaard, B., Rasmussen, Å. K., Vilsbøll, T., & Watt, T. (2018a). How should thyroid-related quality of life be assessed? Recalled patient-reported outcomes compared to here-and-now measures. *Thyroid*, *28*(12), 1561-1570. https://doi.org/10.1089/thy.2018.0210
13. Boesen, V. B., Nissen, S. B., Groenvold, M., Bjorner, J. B., Hegedüs, L., Bonnema, S. J., Rasmussen, Å. K., Feldt-Rasmussen, U., & Watt, T. (2018b). Conversion of standard retrospective patient-reported outcomes

to momentary versions: cognitive interviewing reveals varying degrees of momentary compatibility. *Quality of Life Research*, *27*(4), 1065-1076. https://doi.org/10.1007/s11136-017-1762-7

14. Broniarczyk-Czarniak, M. (2017). Zaburzenia psychiczne współistniejące z chorobą Hashimoto—przegląd piśmiennictwa [The prevalence of psychiatric disorders in patients with Hashimoto's thyroiditis: a literature review]. *Psychiatria*, *14*(4), 209-216.
15. Caputo, A. (2013). Health demand in primary care context: What do people think about physicians?. *Psychology, health & medicine, 18*(2), 145-154. https://doi.org/10.1080/13548506.2012.687828
16. Caputo, A. (2014). Exploring quality of life in Italian patients with rare disease: A computer-aided content analysis of illness stories. *Psychology, Health & Medicine, 19*(2), 211-221. https://doi.org/10.1080/13548506.2013.793372
17. Caputo, A. (2019a). Psychodynamic insights from narratives of people with amyotrophic lateral sclerosis: A qualitative phenomenological study. *Mediterranean Journal of Clinical Psychology*, *7*(2). https://doi.org/10.6092/2282-1619/2019.7.2009.
18. Caputo, A. (2019b). The Experience of Therapeutic Community: Emotional and Motivational Dynamics of People with Drug Addiction Following Rehabilitation. *International Journal of Mental Health and Addiction, 17*(1), 151-165. https://doi.org/10.1007/s11469-018-0008-4
19. Caputo, A. (2020). Illness and object relations: Narratives from women with pulmonary hypertension. *Iranian Journal of Psychiatry and Clinical Psychology, 26*(1), 130-141. https://doi.org/10.32598/ijpcp.26.1.3124.1
20. Carr-Hill, R. A. (1992). Health related quality of life measurement—Euro style. *Health Policy*, *20*(3), 321-328. https://doi.org/10.1016/0168-8510(92)90164-7
21. Carta, M. G., Loviselli, A., Hardoy, M. C., Massa, S., Cadeddu, M., Sardu, C., Carpiniello, B., Dell'Osso, L., & Mariotti, S. (2004). The link between thyroid autoimmunity (antithyroid peroxidase autoantibodies) with anxiety and mood disorders in the community: a field of interest for public health in the future. *BMC psychiatry*, *4*, 25. https://doi.org/10.1186/1471-244X-4-25
22. Castelnuovo, G., Pietrabissa, G., Manzoni, G. M., Corti, S., Ceccarini, M., Borrello, M., Giusti, E. M., Novelli, M., Cattivelli, R., Middleton, N. A., Simpson, S. G., & Molinari, E. (2015). Chronic care management of globesity: promoting healthier lifestyles in traditional and mHealth based settings. *Frontiers in Psychology*, *6*, 1557. https://doi.org/10.3389/fpsyg.2015.01557
23. Catalano, A., Martino, G., Bellone, F., Gaudio, A., Lasco, C., Langher, V., Lasco, A., & Morabito, N. (2018). Anxiety levels predict fracture risk in postmenopausal women assessed for osteoporosis. *Menopause*, *25*(10), 1110-1115. https://doi.org/10.1097/GME.0000000000001123
24. Catalano, A., Martino, G., Bellone, F., Papalia, M., Lasco, C., Basile, G., Sardella, A., Nicocia, G., Morabito, N., & Lasco, A. (2019). Neuropsychological assessment in elderly men with benign prostatic hyperplasia treated with dutasteride. *Clinical drug investigation*, *39*(1), 97-102. https://doi.org/10.1007/s40261-018-0720-7
25. Catalano, A., Martino, G., Morabito, N., Scarcella, C., Gaudio, A., Basile, G., & Lasco, A. (2017). Pain in osteoporosis: from pathophysiology to therapeutic approach. *Drugs & aging*, *34*(10), 755-765. https://doi.org/10.1007/s40266-017-0492-4

26. Catalano, A., Sardella, A., Bellone, F., Lasco, C. G., Martino, G., & Morabito, N. (2020). Executive functions predict fracture risk in postmenopausal women assessed for osteoporosis. *Aging clinical and experimental research*, *32*(11), 2251-2257. https://doi.org/10.1007/s40520-019-01426-w
27. Ciprandi, G., Natoli, V., Puccinelli, P., Incorvaia, C., & Italian Cometa Study Group (2017). Allergic rhinitis: the eligible candidate to mite immunotherapy in the real world. *Allergy, asthma, and clinical immunology: Official journal of the Canadian Society of Allergy and Clinical Immunology*, *13*, 11. https://doi.org/10.1186/s13223-017-0185-x
28. Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Lawrence Erlbaum.
29. Conversano, C., & Di Giuseppe, M. (2021). Psychological factors as determinants of chronic conditions: clinical and psychodynamic advances. *Frontiers in Psychology, 12*, 635708. https://doi.org/10.3389/fpsyg.2021.635708
30. Conversano, C., Di Giuseppe, M., Miccoli, M., Ciacchini, R., Di Silvestre, A., Lo Sterzo, R., Gemignani, A., & Orrù, G. (2020a). Retrospective analyses of psychological distress and defense style among cancer patients. *Clinical Neuropsychiatry*, *17*(4), 217-224. https://doi.org/10.36131/cnfioritieditore20200403
31. Conversano, C., Marchi, L., & Miniati, M. (2020b). Psychological distress among healthcare professionals involved in the covid-19 emergency: Vulnerability and resilience factors. *Clinical Neuropsychiatry*, *17*(2). https://doi.org/10.36131/CN20200212
32. Cooper, D. S., & Biondi, B. (2012). Subclinical thyroid disease. *The Lancet*, *379*(9821), 1142-1154. https://doi.org/10.1016/S0140-6736(11)60276-6
33. Craparo, G., Gori, A., Dell'Aera, S., Costanzo, G., Fasciano, S., Tomasello, A., & Vicario, C. M. (2016). Impaired emotion recognition is linked to alexithymia in heroin addicts. *PeerJ*, *4*, e1864. https://doi.org/10.7717/peerj.1864
34. Crisanti, P., Omri, B., Hughes, E. J., Meduri, G., Hery, C., Clauser, E., Jacquemin, C., & Saunier, B. (2001). The expression of thyrotropin receptor in the brain. *Endocrinology*, *142*(2), 812-822. https://doi.org/10.1210/endo.142.2.7943
35. Dayan, C. M., & Panicker, V. (2013). Hypothyroidism and depression. *European Thyroid Journal*, *2*(3), 168-179. https://doi.org/10.1159/000353777
36. Di Giuseppe, M., Ciacchini, R., Micheloni, T., Bertolucci, I., Marchi, L., & Conversano, C. (2018). Defense mechanisms in cancer patients: A systematic review. *Journal of psychosomatic research, 115*, 76-86. https://doi.org/10.1016/j.jpsychores.2018.10.016
37. Di Giuseppe, M., Di Silvestre, A., Lo Sterzo, R., Hitchcott, P., Gemignani, A., & Conversano, C. (2019). Qualitative and quantitative analysis of the defensive profile in breast cancer women: A pilot study. *Health psychology open*, *6*(1), 20. https://doi.org/10.1177/2055102919854667
38. Di Giuseppe, M., Miniati, M., Miccoli, M., Ciacchini, R., Orrù, G., Lo Sterzo, R., Di Silvestre, A., & Conversano, C. (2020). Defensive responses to stressful life events associated with cancer diagnosis. *Mediterranean Journal of Clinical Psychology, 8(*1). https://doi.org/10.6092/2282-1619/mjcp-2384.
39. Di Giuseppe, M., Perry, J.C., Petraglia, J., Janzen, J., & Lingiardi, V. (2014). Development of a Q-sort version of the defense mechanisms rating scales (DMRS-Q) for clinical use. *Journal of Clinical Psychology, 70*, 452-465. https://doi.org/10.1002/jclp.22089

40. Djurovic, M., Pereira, A. M., Smit, J. W., Vasovic, O., Damjanovic, S., Jemuovic, Z., Pavlovic, D., Miljic, D., Pekic, S., Stojanovic, M., Asanin, M., Krljanac, G., & Petakov, M. (2018). Cognitive functioning and quality of life in patients with Hashimoto thyroiditis on long-term levothyroxine replacement. *Endocrine, 62*(1), 136-143. https://doi.org/10.1007/s12020-018-1649-6

41. Fava, G. A., Tomba, E., & Sonino, N. (2012). Clinimetrics: the science of clinical measurements. *International journal of clinical practice*, *66*(1), 11-15. https://doi.org/10.1111/j.1742-1241.2011.02825.x

42. Ghisi, M., Flebus, G.B., Montano, A., Sanavio, E., & Sica, C. (2006). L'adattamento italiano del BDI-II [Italian adaptation of BDI-II]. In A.T. Beck, R.A. Steer, & G.K. Brown (Eds.), *Beck Depression Inventory-II*. Organizzazioni Speciali.

43. Grabe, H. J., Volzke, H., Ludemann, J., Wolff, B., Schwahn, C., John, U., Meng, W., & Freyberger, H. J. (2005). Mental and physical complaints in thyroid disorders in the general population. *Acta Psychiatrica Scandinavica*, *112*(4), 286-293. https://doi.org/10.1111/j.1600-0447.2005.00586.x

44. Gugliandolo, M. C., Costa, S., Cuzzocrea, F., Larcan, R., & Martino, G. (2020). Adolescents and Body Uneasiness: the Contribution of Supportive Parenting and Trait Emotional Intelligence. *Journal of Child and Family Studies*, *29*(9), 2453-2462. https://doi.org/10.1007/s10826-020-01779-1

45. Hamilton, M. A. X. (1959). The assessment of anxiety states by rating. *British journal of medical psychology, 32*(1), 50-55. https://doi.org/10.1111/j.2044-8341.1959.tb00467.x

46. Hasegawa, C., Kawai, T., Tanaka, M., & Fukao, A. (2019). Psychological characteristics of surgical patients with thyroid disease. *Psychologia, 60*(4), 217-232. https://doi.org/10.2117/psysoc.2019-B006

47. Haugen, B. R., Alexander, E. K., Bible, K. C., Doherty, G. M., Mandel, S. J., Nikiforov, Y. E., Pacini, F., Randolph, G. W., Sawka, A. M., Schlumberger, M., Schuff, K. G., Sherman, S. I., Sosa, J. A., Steward, D. L., Tuttle, R. M., & Wartofsky, L. (2016). 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. *Thyroid*, *26*(1), 1-133. https://doi.org/10.1089/thy.2015.0020

48. Ivanova, G. P., & Gorobets, L. N. (2011). Psychological aspects of systemic approach to diagnostics of mental and immunological disorders in diffuse-nodular form of Hashimoto's thyroiditis. *Zhurnal nevrologii i psikhiatrii imeni SS Korsakova*, *111*(11 Pt 1), 10-16.

49. Kelly, R. R., McDonald, L. T., Jensen, N. R., Sidles, S. J., & LaRue, A. C. (2019). Impacts of psychological stress on osteoporosis: clinical implications and treatment Interactions. *Frontiers in psychiatry*, *10*, 200. https://doi.org/10.3389/fpsyt.2019.00200

50. Le Donne, M., Settineri, S., & Benvenga, S. (2012). Early pospartum alexithymia and risk for depression: relationship with serum thyrotropin, free thyroid hormones and thyroid autoantibodies. *Psychoneuroendocrinology*, *37*(4), 519-533. https://doi.org/10.1016/j.psyneuen.2011.08.001

51. Lenzo, V., Sardella, A., Martino, G., & Quattropani, M. C. (2020). A systematic review of metacognitive beliefs in chronic medical conditions. *Frontiers in Psychology, 10*, 2875. https://doi.org/10.3389/fpsyg.2019.02875

52. Lucifora, C., Martino, G., Curcuruto, A., Salehinejad, M. A., & Vicario, C. M. (2021). How Self-Control Predicts Moral Decision Making: An Exploratory Study on Healthy Participants. *International Journal of Environmental Research and Public Health*, *18*(7), 3840. https://doi.org/10.3390/ijerph18073840
53. Marazziti, D., Golia, F., Picchetti, M., Pioli, E., Mannari, P., Lenzi, F., Conversano, C., Carmassi, C., Catena Dell'Osso, M., Consoli, G., Baroni, S., Giannaccini, G., Zanda, G., & Dell'Osso, L. (2008). Decreased density of the platelet serotonin transporter in pathological gamblers. *Neuropsychobiology*, *57*(1-2), 38–43. https://doi.org/10.1159/000129665
54. Marchini, F., Caputo, A., Balonan, J. T., Fedele, F., Langher, V., & Napoli, A. (2020). Emotional Dynamics of Persons with Type 2 Diabetes and Their Potential Role in Treatment Adherence: Insights from a Clinical Psychodynamic Perspective. *Psychology Hub*, *37*(2), 23-30. https://doi.org/10.13133/2724-2943/17160
55. Marchini, F., Caputo, A., Napoli, A., Balonan, J. T., Martino, G., Nannini, V., & Langher, V. (2018). Chronic illness as loss of good self: underlying mechanisms affecting diabetes adaptation. *Mediterranean Journal of Clinical Psychology*, *6*(3). https://doi.org/10.6092/2282-1619/2018.6.1981
56. Markomanolaki, Z. S., Tigani, X., Siamatras, T., Bacopoulou, F., Tsartsalis, A., Artemiadis, A., Megalooikonomou, V., Vlachakis, D., Chrousos, G. P., & Darviri, C. (2019). Stress Management in Women with Hashimoto's thyroiditis: A Randomized Controlled Trial. *Journal of molecular biochemistry*, *8*(1), 3–12.
57. Martino, G., Bellone, F., Langher, V., Caputo, A., Catalano, A., Quattropani, M. C., & Morabito, N. (2019a). Alexithymia and psychological distress affect perceived quality of life in patients with type 2 diabetes mellitus. *Mediterranean Journal of Clinical Psychology*, *7*(3). https://doi.org/10.6092/2282-1619/2019.7.2328.
58. Martino, G., Caputo, A., Bellone, F., Quattropani, M. C., & Vicario, C. M. (2020a). Going Beyond the Visible in Type 2 Diabetes Mellitus: Defense Mechanisms and their Associations with Depression and Health-Related Quality of Life. *Frontiers in Psychology*, *11*, 267. https://doi.org/10.3389/fpsyg.2020.00267
59. Martino, G., Caputo, A., Schwarz, P., Bellone, F., Fries, W., Quattropani, M. C., & Vicario, C. M. (2020b). Alexithymia and inflammatory bowel disease: A systematic review. *Frontiers in Psychology*, 11, 1763. https://doi.org/10.3389/fpsyg.2020.01763
60. Martino, G., Caputo, A., Vicario, C. M., Catalano, A., Schwarz, P., & Quattropani, M. C. (2020c). The relationship between alexithymia and type 2 diabetes: a systematic review. *Frontiers in Psychology*, *11*, 2026. https://doi.org/10.3389/fpsyg.2020.02026
61. Martino, G., Caputo, A., Vicario, C.M., Feldt-Rasmussen, U., Watt, T., Quattropani, M.C., Benvenga, S., & Vita, R. (2021). Alexithymia, Emotional Distress and Perceived Quality of Life in Patients with Hashimoto's Thyroiditis. *Frontiers in Psychology*, 12, 667237. https://doi.org/10.3389/fpsyg.2021.667237.
62. Martino, G., Catalano, A., Agostino, R. M., Bellone, F., Morabito, N., Lasco, C. G., Vicario, C. M., Schwarz, P., & Feldt-Rasmussen, U. (2020d). Quality of life and psychological functioning in postmenopausal women undergoing aromatase inhibitor treatment for early breast cancer. *PloS One, 15*(3), e0230681. https://doi.org/10.1371/journal.pone.0230681
63. Martino, G., Catalano, A., Bellone, F., Langher, V., Lasco, C., Penna, A., Nicocia, G., & Morabito, N. (2018a). Quality of life in postmenopausal women: Which role for vitamin D?. *Mediterranean Journal of Clinical Psychology*, *6*(2). https://doi.org/10.6092/2282-1619/2018.6.1875

64. Martino, G., Catalano, A., Bellone, F., Russo, G. T., Vicario, C. M., Lasco, A., Quattropani, M. C., & Morabito, N. (2019b). As time goes by: Anxiety negatively affects the perceived quality of life in patients with Type 2 diabetes of long duration. *Frontiers in Psychology, 10*, 1779. https://doi.org/10.3389/fpsyg.2019.01779.
65. Martino, G., Catalano, A., Bellone, F., Sardella, A., Lasco, C., Caprì, T., Langher, V., Caputo, A., Fabio, R. A. & Morabito, N. (2018b). Vitamin D status is associated with anxiety levels in postmenopausal women evaluated for osteoporosis. *Mediterranean Journal of Clinical Psychology*, *6*(1). https://doi.org/10.6092/2282-1619/2018.6.1740
66. Martino, G., Langher, V., Cazzato, V., & Vicario, C. M. (2019c). Psychological factors as determinants of medical conditions. *Frontiers in psychology*, *10*, 2502. https://doi.org/10.3389/fpsyg.2019.02502/full
67. Martino, G., Sardella, A., Bellone, F., Lasco, C., Langher, V., Cazzato, V., Penna, A., Vicario, C., Morabito, N., & Catalano, A. (2019d). Executive functions and bone health: a focus on cognitive impulsivity and bone mineral density. *Mediterranean Journal of Clinical Psychology*, *7*(2). https://doi.org/10.6092/2282-1619/2019.7.2167
68. Merlo, E. M. (2019). Opinion article: The role of psychological features in chronic diseases, advances and perspectives. *Mediterranean Journal of Clinical Psychology, 7*(3). https://doi.org/10. 6092/2282-1619/2019.7.2341.
69. Mizokami, T., Wu Li, A., El-Kaissi, S., & Wall, J. R. (2004). Stress and thyroid autoimmunity. *Thyroid, 14*(12), 1047-1055. https://doi.org/10.1089/thy.2004.14.1047
70. Moncayo, R., & Moncayo, H. (2014). Exploring the aspect of psychosomatics in hypothyroidism: the WOMED model of body–mind interactions based on musculoskeletal changes, psychological stressors, and low levels of magnesium. *Woman-Psychosomatic Gynaecology and Obstetrics*, *1*, 1-11. https://doi.org/10.1016/j.woman.2014.02.001
71. Montagna, G., Imperiali, M., Agazzi, P., D'Aurizio, F., Tozzoli, R., Feldt-Rasmussen, U., & Giovanella, L. (2016). Hashimoto's encephalopathy: A rare proteiform disorder. *Autoimmunity Reviews*, *15*(5), 466-476. https://doi.org/10.1016/j.autrev.2016.01.014
72. Mula, M., Pini, S., Monteleone, P., Iazzetta, P., Preve, M., Tortorella, A., Amato, E., Di Paolo, L., Conversano, C., Rucci, P., Cassano, G. B., & Maj, M. (2008). Different temperament and character dimensions correlate with panic disorder comorbidity in bipolar disorder and unipolar depression. *Journal of anxiety disorders*, *22*(8), 1421–1426. https://doi.org/10.1016/j.janxdis.2008.02.004
73. Nexo, M. A., Watt, T., Pedersen, J., Bonnema, S. J., Hegedüs, L., Rasmussen, A. K., Feldt-Rasmussen, U., & Bjorner, J. B. (2014). Increased risk of long-term sickness absence, lower rate of return to work, and higher risk of unemployment and disability pensioning for thyroid patients: A Danish register-based cohort study. *The Journal of Clinical Endocrinology & Metabolism*, *99*(9), 3184-3192. https://doi.org/10.1210/jc.2013-4468
74. Palagini, L., Carmassi, C., Conversano, C., Gesi, C., Bazzichi, L., Giacomelli, C., & Dell'Osso, L. (2016). Transdiagnostic factors across fibromyalgia and mental disorders: sleep disturbances may play a key role: A clinical review. *Clinical and experimental rheumatology*, *34*(2 Suppl 96), S140–S144.

75. Patrick, D. L., & Deyo, R. A. (1989). Generic and disease-specific measures in assessing health status and quality of life. *Medical care*, *27*, S217-S232.
76. Patron, E., Benvenuti, S. M., Lopriore, V., Aratari, J., & Palomba, D. (2017). Somatic-affective, but not cognitive-depressive symptoms are associated with reduced health–related quality of life in patients with congestive heart failure. *Psychosomatics*, *58*(3), 281-291. https://doi.org/10.1016/j.psym.2017.01.001
77. Piccinni, A., Origlia, N., Veltri, A., Vizzaccaro, C., Marazziti, D., Catena-Dell'osso, M., Conversano, C., Moroni, I., Domenici, L., & Dell'osso, L. (2012). Plasma β-amyloid peptides levels: a pilot study in bipolar depressed patients. *Journal of affective disorders*, *138*(1-2), 160–164. https://doi.org/10.1016/j.jad.2011.12.042
78. Quattropani, M. C., Lenzo, V., Filastro, A., & Fries, W. (2019). Metacognitions and basic emotions in patients with irritable bowel syndrome and inflammatory bowel disease. *Psicoterapia Cognitiva e Comportamentale*, *25*(1), 35-51.
79. Rafanelli, C., Roncuzzi, R., Finos, L., Tossani, E., Tomba, E., Mangelli, L., Urbinati, S., Pinelli, G., & Fava, G. A. (2003). Psychological assessment in cardiac rehabilitation. *Psychotherapy and Psychosomatics*, *72*(6), 343-349. https://doi.org/10.1159/000073031
80. Randazzo, C. L., Pino, A., Ricciardi, L., Romano, C., Comito, D., Arena, E., Saitta, S., & Caggia, C. (2015). Probiotic supplementation in systemic nickel allergy syndrome patients: study of its effects on lactic acid bacteria population and on clinical symptoms. *Journal of applied microbiology, 118*(1), 202–211. https://doi.org/10.1111/jam.12685
81. Rieben, C., Segna, D., da Costa, B. R., Collet, T. H., Chaker, L., Aubert, C. E., Baumgartner, C., Almeida, O. P., Hogervorst, E., Trompet, S., Masaki, K., Mooijaart, S. P., Gussekloo, J., Peeters, R. P., Bauer, D. C., Aujesky, D., & Rodondi, N. (2016). Subclinical thyroid dysfunction and the risk of cognitive decline: A meta-analysis of prospective cohort studies. *The Journal of Clinical Endocrinology & Metabolism*, *101*(12), 4945-4954. https://doi.org/10.1210/jc.2016-2129
82. Rosa, V., Tomai, M., Lauriola, M., Martino, G., & Di Trani, M. (2019). Body mass index, personality traits, and body image in Italian pre-adolescents: An opportunity for overweight prevention. *Psihologija*, *52*(4), 379-393. https://doi.org/10.2298/PSI181121009R
83. Samuels, M. H. (2008). Cognitive function in untreated hypothyroidism and hyperthyroidism. *Current Opinion in Endocrinology, Diabetes and Obesity*, *15*(5), 429-433. https://doi.org/10.1097/MED.0b013e32830eb84c.
84. Settineri, S., Frisone, F., Merlo, E. M., Geraci, D., & Martino, G. (2019). Compliance, adherence, concordance, empowerment, and self-management: Five words to manifest a relational maladjustment in diabetes. *Journal of multidisciplinary healthcare*, *12*, 299-314. https://doi.org/10.2147/JMDH.S193752
85. Thvilum, M., Brandt, F., Brix, T. H., & Hegedüs, L. (2014). Hypothyroidism is a predictor of disability pension and loss of labor market income: a Danish register-based study. *The Journal of Clinical Endocrinology & Metabolism*, *99*(9), 3129-3135. https://doi.org/10.1210/jc.2014-1407
86. Tomai, M., & Lauriola, M., & Caputo, A. (2018). Are social support and coping styles differently associated with adjustment to cancer in early and advanced stages?. *Mediterranean Journal of Clinical Psychology, 7*(1). https://doi.org/10.6092/2282-1619/2019.7.19831981

87. Van Houtum, L., Rijken, M., & Groenewegen, P. (2015). Do everyday problems of people with chronic illness interfere with their disease management?. *BMC public health*, *15*(1), 1000. https://doi.org/10.1186/s12889-015-2303-3

88. Veltri, A., Scarpellini, P., Piccinni, A., Conversano, C., Giacomelli, C., Bombardieri, S., Bazzichi, L., & Dell'Osso, L. (2012). Methodological approach to depressive symptoms in fibromyalgia patients. *Clinical and experimental rheumatology*, *30*(6 Suppl 74), 136–142.

89. Vicario C. M. (2013). Altered insula response to sweet taste processing in recovered anorexia and bulimia nervosa: a matter of disgust sensitivity?. *The American journal of psychiatry*, *170*(12), 1497. https://doi.org/10.1176/appi.ajp.2013.13060748

90. Vicario, C.M., Martino, G., Marcuzzo, A., & Craparo, G. (2021). No Evidence of Perceptual Pseudoneglect in Alexithymia. *Brain Science, 11,* 376. https://doi.org/10.3390/brainsci11030376

91. Vicario, C. M., Nitsche, M. A., Salehinejad, M. A., Avanzino, L., & Martino, G. (2020). Time Processing, Interoception, and Insula Activation: A Mini-Review on Clinical Disorders. *Frontiers in psychology*, *11*, 1893. https://doi.org/10.3389/fpsyg.2020.01893

92. Vita, R., Caputo, A., Quattropani, M.C., Watt, T., Feldt-Rasmussen, U., Puleio, P., Benvenga, S., & Martino, G. (2020). Quality of Life in Patients with Hyperthyroidism: Where do we stand?. *Mediterranean Journal of Clinical Psychology, 8*(2), 1-28. https://doi.org/10.6092/2282-1619/mjcp-2521.

93. Vita, R., Mazzi, V., Antonelli, A., & Benvenga, S. (2013). Antithyroid medications and psychosis. *Expert opinion on drug safety*, *12*(6), 865-872. https://doi.org/10.1517/14740338.2013.823397

94. Ware, J. E., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Medical Care, 30*(6), 473-483. https://doi.org/10.1097/00005650-199206000-00002

95. Watt, T., Bjorner, J. B., Groenvold, M., Cramon, P., Winther, K. H., Hegedüs, L., Bonnema, S. J., Rasmussen, Å. K., Ware, J. E., Jr, & Feldt-Rasmussen, U. (2015). Development of a short version of the thyroid-related patient-reported outcome ThyPRO. *Thyroid*, *25*(10), 1069-1079. https://doi.org/10.1089/thy.2015.0209

96. Watt, T., Bjorner, J. B., Groenvold, M., Rasmussen, Å. K., Bonnema, S. J., Hegedüs, L., & Feldt-Rasmussen, U. (2009). Establishing construct validity for the thyroid-specific patient reported outcome measure (ThyPRO): An initial examination. *Quality of Life Research*, *18*(4), 483-496. https://doi.org/10.1007/s11136-009-9460-8

97. Watt, T., Cramon, P., Hegedüs, L., Bjorner, J. B., Bonnema, S. J., Rasmussen, Å. K., Feldt-Rasmussen, U., & Groenvold, M. (2014). The thyroid-related quality of life measure ThyPRO has good responsiveness and ability to detect relevant treatment effects. *The Journal of Clinical Endocrinology & Metabolism*, *99*(10), 3708-3717. https://doi.org/10.1210/jc.2014-1322

98. Watt, T., Hegedüs, L., Bjorner, J. B., Groenvold, M., Bonnema, S. J., Rasmussen, Å. K., & Feldt-Rasmussen, U. (2012). Is thyroid autoimmunity per se a determinant of quality of life in patients with autoimmune hypothyroidism?. *European Thyroid Journal*, *1*(3), 186-192. https://doi.org/10.1159/000342623

99. Winther, K. H., Cramon, P., Watt, T., Bjorner, J. B., Ekholm, O., Feldt-Rasmussen, U., Groenvold, M., Rasmussen, Å. K., Hegedüs, L., & Bonnema, S. J. (2016). Disease-Specific as Well as Generic Quality of Life Is Widely Impacted in Autoimmune Hypothyroidism and Improves during the First Six Months of Levothyroxine Therapy. *PloS one*, *11*(6), e0156925. https://doi.org/10.1371/journal.pone.0156925

100. Wong, C. K., Choi, E. P., Woo, Y. C., & Lang, B. H. (2018). Measurement properties of ThyPRO short-form (ThyPRO-39) for use in Chinese patients with benign thyroid diseases. *Quality of Life Research*, *27*(8), 2177-2187. https://doi.org/10.1007/s11136-018-1857-9

101. Wong, C. K., Lang, B. H., & Lam, C. L. (2016). A systematic review of quality of thyroid-specific health-related quality-of-life instruments recommends ThyPRO for patients with benign thyroid diseases. *Journal of Clinical Epidemiology*, *78*, 63-72. https://doi.org/10.1016/j.jclinepi.2016.03.006

102. Yalcin, M. M., Altinova, A. E., Cavnar, B., Bolayir, B., Akturk, M., Arslan, E., Ozkan, C., Cakir, N., & Balos Toruner, F. (2017). Is thyroid autoimmunity itself associated with psychological well-being in euthyroid Hashimoto's thyroiditis?. *Endocrine journal*, *64*(4), 425-429. https://doi.org/10.1507/endocrj.EJ16-0418

103. Yıldız, M., Şahin, Ş., Batmaz, S., Songur, E., & Kutlutürk, F. (2017). The relationship between depression, anxiety, personality traits and coping strategies of patients with euthyroid Hashimoto's Thyroiditis. *The European Journal of Psychiatry*, *31*(3), 113-118. https://doi.org/10.1016/j.ejpsy.2017.06.001

DOI: 10.13129/2282-1619/mjcp-3072